Amendments to the Claims:

This listing of claims will replace all prior versions, and listings of claims in the application:

Listing of Claims:

1.-10. (Canceled)

11. (Currently amended) An apoptotic agent composition that modulates induces apoptosis by binding to a Bcl-2 family member protein and preferentially inducing apoptosis in a cell that over-expresses the Bcl-2 family member protein, the agent composition having the following formula II,

$$\begin{array}{c|c}
R_6 & 0 \\
\hline
 & 1 \\
\hline
 & 2 \\
\hline
 & R_1 \\
\hline
 & 7 \\
\hline
 & 0 \\
\hline
 & 5 \\
\hline
 & 3 \\
\hline
 & R_2 \\
\end{array}$$
(II)

having an absolute configuration of [2R, 3R, 4S, 7S, 8R], and comprising at least a first and a second chemical modification, the first chemical modification decreasing the affinity of the agent for cytochrome B, wherein the first chemical modification is selected from the following:

R₄ is hydrogen, a C₁-C₈ linear or branched alkane, a C₁-C₈ hydroxyalkane, or a substituted alkyl group; and

R₅ is hydrogen, a C₁-C₈ linear or branched alkane, hydroxyl, a C₁-C₈ hydroxyalkane, amino, a C₂-C₈ di- or tri- alkylamine, a C₁-C₈ carboxylic acid, a C₂-C₈ amide, or a substituted alkyl group;

and the second chemical modification is selected from the following: wherein R_1 is hydrogen, a C_1 - C_8 linear or branched alkane, hydroxyl, a C_1 - C_8 hydroxyalkane, amino, a C_1 - C_8 di- or tri-amine, a C_1 - C_8 amide, a C_1 - C_8 carboxylic acid, or a substituted alkyl group;

 R_2 is hydrogen, a C_1 - C_8 linear or branched alkane, hydroxyl, a C_1 - C_8 hydroxyalkane, amino, a C_1 - C_8 di- or tri-amine, a C_1 - C_8 amide, a C_1 - C_8 carboxylic acid, or a substituted alkyl group;

 R_3 is hydrogen, a C_1 - C_8 linear or branched alkane, hydroxyl, a C_1 - C_8 hydroxyalkane, amino, a C_1 - C_8 di- or tri-amine, a C_1 - C_8 amide, a C_1 - C_8 carboxylic acid, or a substituted alkyl group; and

R₄ is hydrogen, a C₁-C₈ linear or branched alkane, a C₁-C₈ hydroxyalkane, or a substituted alkyl group;

R₅ is hydrogen, a C_1 - C_8 linear or branched alkane, hydroxyl, a C_1 - C_8 hydroxyalkane, amino, a C_3 - C_8 di- or tri-alkylamine, a C_1 - C_8 carboxylic acid, a C_2 - C_8 amide, or a substituted alkyl group; and

 R_6 is hydrogen, a C_1 - C_8 linear or branched alkane, hydroxyl, a C_1 - C_8 hydroxyalkane, amino, a C_1 - C_8 di- or tri-amine, a C_1 - C_8 amide, a C_1 - C_8 carboxylic acid, or a substituted alkyl group.

- 12. (Currently amended) The agent composition of claim 11, further comprising a pharmaceutically acceptable carrier.
- 13. (Currently amended) The agent composition of claim 11 for use in treating an apoptosis-associated disease in a subject in need thereof.
 - 14. (Canceled)
- 15. (Currently amended) A method for identifying an agent a composition which modulates induces apoptosis of a cell by binding wherein the composition binds to the hydrophobic pocket of an anti-apoptotic Bcl-x_L or Bcl-2 family member protein formed by the BH1, BH2 and BH3 domains of the protein, comprising:
- a) admixing a candidate compound with a cell which over-expresses the antiapoptotic Bcl-x_L or Bcl-2 family member protein;

- b) admixing the candidate compound with a control cell which does not overexpress the anti-apoptotic $\underline{Bcl-x_L}$ or $\underline{Bcl-2}$ -family member protein; and
- c) determining whether the candidate compound modulates induces the activity of the anti-apoptotic Bcl-x_L or Bcl-2 family member protein to produce a physiological change in the cell which over-expresses the anti-apoptotic Bcl-x_L or Bcl-2 family member protein indicative of apoptosis, but does not produce a substantial physiological change in the cell which does not over-express the anti-apoptotic Bcl-x_L or Bcl-2 family member protein.

16. (Canceled)

- 17. (Original) The method of claim 15, wherein the physiological change indicative of apoptosis is cell shrinkage, chromosome condensation and migration, mitochondrial swelling, or disruption of mitochondrial transmembrane potential.
- 18. (Original) The method of claim 17, wherein the cellular change comprises disruption of mitochondrial transmembrane potential.
- 19. (Currently amended) The method of claim 15, wherein the cell that over-expresses the anti-apoptotic Bcl-x_L or Bcl-2 family member protein is transfected with a gene which encodes the anti-apoptotic Bcl-x_L or Bcl-2-protein.

20. (Canceled)

21. (Currently amended) The A method of claim 20 for treating a subject having an apoptosis-associated disease, comprising administering to the subject a therapeutically effective amount of a wherein the antimycin or antimycin derivative is of the following formula, and having an absolute configuration of [2R, 3R, 4S, 7S, 8R]:

wherein R_1 is hydrogen, a C_1 - C_8 linear or branched alkane, hydroxyl, a C_1 - C_8 hydroxyalkane, amino, a C_1 - C_8 di- or tri-amine, a C_1 - C_8 amide, a C_1 - C_8 carboxylic acid, or a substituted alkyl group;

 R_2 is hydrogen, a C_1 - C_8 linear or branched alkane, hydroxyl, a C_1 - C_8 hydroxyalkane, amino, a C_1 - C_8 di- or tri-amine, a C_1 - C_8 amide, a C_1 - C_8 carboxylic acid, or a substituted alkyl group;

 R_3 is hydrogen, a C_1 - C_8 linear or branched alkane, hydroxyl, a C_1 - C_8 hydroxyalkane, amino, a C_1 - C_8 di- or tri-amine, a C_1 - C_8 amide, a C_1 - C_8 carboxylic acid, or a substituted alkyl group;

R₄ is hydrogen, a C₁-C₈ linear or branched alkane, hydroxyl, a C₁-C₈ carboxylic acid, or a substituted alkyl group;

 R_5 is hydrogen, a C_1 - C_8 linear or branched alkane, hydroxyl, a C_1 - C_8 hydroxyalkane, amino, a C_1 - C_8 di- or tri-alkylamine, a C_1 - C_8 amide, a C_1 - C_8 carboxylic acid, or a substituted alkyl group; and

 R_6 is hydrogen, a C_1 - C_8 linear or branched alkane, hydroxyl, a C_1 - C_8 hydroxyalkane, amino, a C_1 - C_8 di- or tri-amine, a C_1 - C_8 amide, a C_1 - C_8 carboxylic acid, or a substituted alkyl group.

22. (Original) The method of claim 21, wherein the antimycin derivative is 2-methoxy ether antimycin A or A₃.

23. (Canceled)

- 24. (Currently amended) The method of claim 20 21, wherein the subject is human.
- 25. (Currently amended) The method of claim 20 21, further comprising administering a pharmaceutical carrier.
- 26. (Currently amended) The method of claim 20 21, wherein the administration is intravenous, subcutaneous, intramuscular, intradermal, transdermal, intrathecal, intracerebral, intraperitoneal, epidural or oral.